

## PATENT COOPERATION TREATY



## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CP60845	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/FR2003/003542	International filing date (day/month/year) 01 décembre 2003 (01.12.2003)	Priority date (day/month/year) 02 décembre 2002 (02.12.2002)
International Patent Classification (IPC) or national classification and IPC C07C 229/22		
Applicant CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

This report is also accompanied by ANNEXES. i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of \_\_\_\_\_ sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability: citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 07 juillet 2004 (07.07.2004)	Date of completion of this report 07 March 2005 (07.03.2005)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/FR2003/003542

## I. Basis of the report

## 1. With regard to the elements of the international application:\*

- the international application as originally filed
- the description:

pages I-38 . as originally filed  
 pages \_\_\_\_\_ . filed with the demand  
 pages \_\_\_\_\_ . filed with the letter of \_\_\_\_\_

- the claims:

pages 1-18 . as originally filed  
 pages \_\_\_\_\_ . as amended (together with any statement under Article 19)  
 pages \_\_\_\_\_ . filed with the demand  
 pages \_\_\_\_\_ . filed with the letter of \_\_\_\_\_

- the drawings:

pages 1/2-2/22-18 . as originally filed  
 pages \_\_\_\_\_ . filed with the demand  
 pages \_\_\_\_\_ . filed with the letter of \_\_\_\_\_

- the sequence listing part of the description:

pages \_\_\_\_\_ . as originally filed  
 pages \_\_\_\_\_ . filed with the demand  
 pages \_\_\_\_\_ . filed with the letter of \_\_\_\_\_

## 2. With regard to the language. all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).  
 the language of publication of the international application (under Rule 48.3(b)).  
 the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

## 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application. the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.  
 filed together with the international application in computer readable form.  
 furnished subsequently to this Authority in written form.  
 furnished subsequently to this Authority in computer readable form.  
 The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
 The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4.  The amendments have resulted in the cancellation of:

- the description. pages \_\_\_\_\_  
 the claims. Nos. \_\_\_\_\_  
 the drawings. sheets/fig \_\_\_\_\_

5.  This report has been established as if (some of) the amendments had not been made. since they have been considered to go beyond the disclosure as filed. as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

**Supplemental Box**  
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV.4

Claim 1 claims a method for preparing a compound (I), which method includes the reduction of an isoxazole derivative having formula (II). The preparation includes either:

1. the reduction of compound (II) under conditions that lead directly to derivatives having formula (I),  
or
2. the reduction of compound (II) under conditions that lead to the production of at least one lactone having formula (III).

The technical features that link these two methods consist of the compounds of formulae (I) and (II).

However, the starting materials of formula (II) and the materials of formula (I) are known from D1 (see the passages in Box V hereinafter).

As a result, the present Authority considers that the claims cover the following two groups of inventions:

- I. Claims 1, 12-16 and 18 (all in part) relate to a method for preparing a compound (I), which method includes the reduction of an isoxazole derivative having formula (II). The preparation includes the reduction of compound (II) under conditions that lead directly to derivatives having formula (I).
- II. Claims 1 (in part), 2-11, 12-16 (in part), 17 and

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**Supplemental Box**  
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: IV. 4

18 (in part) relate to a method for preparing a compound (I), which method includes the reduction of an isoxazole derivative having formula (II). The preparation includes the reduction of compound (II) under conditions that lead to the production of at least one lactone having formula (III).

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## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	2-18	YES
	Claims	1	NO
Inventive step (IS)	Claims	2-11, 17, 18	YES
	Claims	12-16	NO
Industrial applicability (IA)	Claims	1-18	YES
	Claims		NO

## 2. Citations and explanations

D1: CAPLAN J F ET AL: "Vinylogous Amide Analogues of Diaminopimelic Acid (DAP) as Inhibitors of Enzymes Involved in Bacterial Lysine Biosynthesis" ORGANIC LETTERS, vol. 2, no. 24, 10 November 2000 (2000-11-10), pages 3857-3860, XP002247986 WASHINGTON DC.

## 1. Novelty (PCT Article 33(2)):

1.1 D1 discloses (diagram 2, page 3858, reaction of 11->12) a method for preparing a compound (I), which method includes the reduction of an isoxazole derivative having formula (II). The preparation includes the reduction of compound (II) under conditions that lead directly to derivatives having formula (I).

As a result, D1 deprives independent claim 1 of novelty.

1.2 Claims 2-16 are dependent claims are therefore considered to be novel (PCT Article 33(2)).

1.3 The subject matter of claims 17 and 18 is not

disclosed in D1 and can consequently be considered to be novel.

**2. Inventive step (PCT Article 33(3)):**

2.1 In light of D1, the technical problem can be considered to be that of providing an enhanced method for synthesising compounds of formula (I).

The solution proposed by the applicant consists of the methods as per claims 12-16.

Claims 12-16 differ from D1 in that they claim methods for synthesising starting material (II) of claim 1.

However, the synthesis of an isoxazole from a compound (VI), as well as the synthesis of a compound (VI) from a compound (VII) are considered to be part of the general knowledge of, and be well known to, a person skilled in the art.

A person skilled in the art, aware of D1 and on the basis of his/her general knowledge, could arrive at the subject matter of claims 12-16 without having to exercise any inventive skill.

As a result, the subject matter of claims 12-16 does not fulfil the requirements set forth in PCT Article 33(3).

2.2 The reaction conditions in claims 2-11 are not disclosed or suggested in D1 or D2. It follows that the method in claims 2-11 constitutes an alternative method. Since there is nothing in the prior art

that could lead a person skilled in the art to the subject matter of claims 2-11, the subject matter of said claims is considered to be inventive.

- 2.3 Since the subject matter of claim 17 does not appear to include the operating conditions necessary for producing material (III), said subject matter cannot be considered to fulfil the requirements of PCT Article 33(3).
- 2.4 The compounds in claim 18 are intermediates in the synthesis method as per claims 9 and 17. Since these compounds also make an important contribution to the structure of the material, they can likewise be considered to involve an inventive step.

**3. PCT Article 6:**

- 3.1 It is clear from the description and figures 1 and 2 that the synthesis of (I) from (II) and via (III) requires the use of very specific reagents or series of reagents. The claims, however, do not claim the operating conditions necessary for carrying out the method, in particular, the conditions necessary for producing compounds (III).

It follows that claims 1-17 do not fulfil the requirements set forth in PCT Article 6.

- 3.2 The method of the present invention as per independent claim 1 uses the compounds of formula (II) as the starting material. The part of dependent claim 9 that relates to the synthesis of materials (IV) and (V) from compound (VI) is, therefore, inconsistent with the subject matter of

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claim 1.

The subject matter of claim 9 lacks clarity.